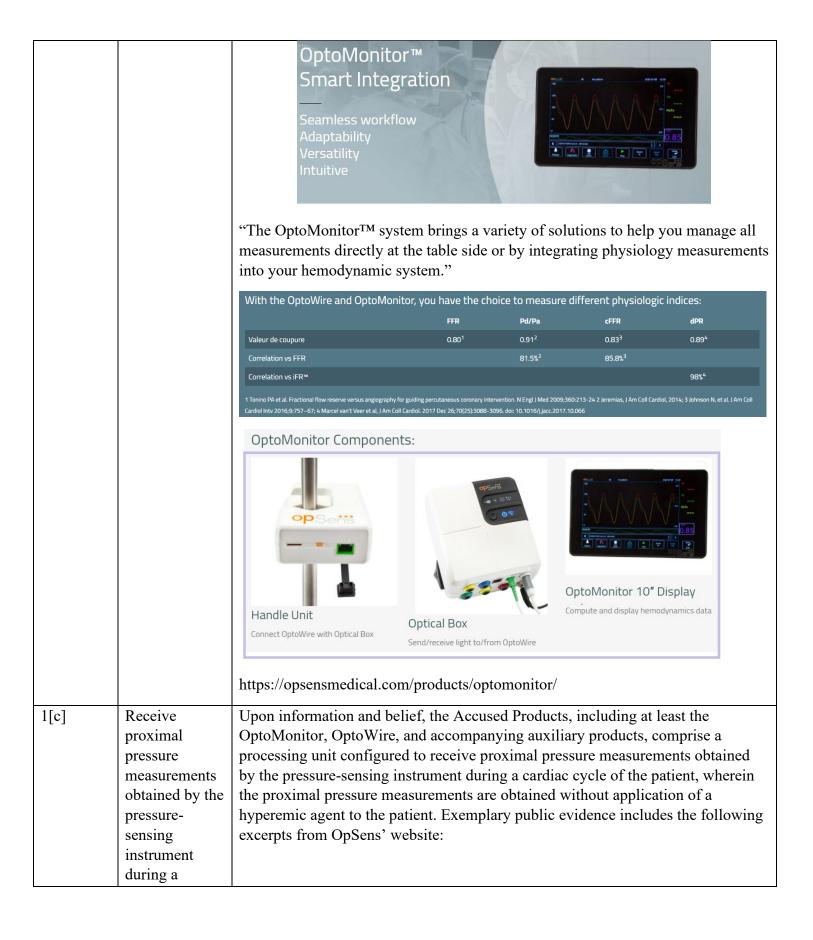
# **Exhibit D**

### Accused Products: System Including (Method Using) at Least OptoWire and **OptoMonitor And Accompanying Auxiliary Products** U.S. 10,912,463 (Davies '463) Claim Terms Exemplary Representative Evidence from Defendants Claim in US 10,912,463 1[pre] A system for Upon information and belief, the Accused Products, including at least the evaluating a OptoMonitor, OptoWire, and accompanying auxiliary products, comprise a stenosis of a system for evaluating assessing a stenosis of a vessel of a patient. Exemplary vessel of a public evidence includes the following excerpts from OpSens' website: patient, the OpSens OptoWire is a modern pressure system comprising: guidewire designed to assess stenoses in vessels such as coronary arteries. OptoWire is powered by Fidela™, a patented 2<sup>nd</sup> generation fiber optic sensor to measure physiologic indices including Fractional Flow Reserve (FFR and diastolic Pressure Ratio (dPR). MORE INFORMATION https://opsensmedical.com/products/optowire/ With the OptoWire and OptoMonitor, you have the choice to measure different physiologic indices: Pd/Pa $0.80^{1}$ 0.91<sup>2</sup> 0.833 0.894 Valeur de coupure Correlation vs FFR 81.5%<sup>2</sup> 85.8%<sup>3</sup> Correlation vs iFR™ 1 Tonino PA et al. Fractional flow reserve versus angiography for guiding percutaneous coronary intervention. N Engl J Med 2009;360:213-24 2 Jeremias, J Am Coll https://opsensmedical.com/products/optomonitor/

#### "5.6 INDICATIONS FOR USE To measure pressure in blood vessels including both coronary and peripheral vessels, during diagnostic angiography and/or any interventional procedures. Blood pressure measurements provide hemodynamic information, such as fractional flow reserve, for the diagnosis and treatment of blood vessel disease." OpSens Submission for FDA Approval, Complaint Exhibit C, p. 5. Upon information and belief, the Accused Products, including at least the 1[a] A pressuresensing guide OptoMonitor, OptoWire, and accompanying auxiliary products, comprise a wire sized and pressure-sensing guide wire sized and shaped for introduction into the vessel of shaped for the patient, the pressure-sensing guide wire comprising a proximal portion, a distal introduction portion, and a pressure monitoring element coupled to the distal portion. into the vessel Exemplary public evidence includes the following excerpts from OpSens' website: of the patient, the pressuresensing guide wire comprising a OptoWire™ proximal 2<sup>nd</sup> Generation portion, a Fiber Optic distal portion, and a pressure The Lowest Drift in the Industry monitoring element coupled to the distal portion; "OptoWire OpSens OptoWire is a modern pressure guidewire designed to assess stenoses in vessels such as coronary arteries."

		https://opsensmedical.com/products/optowire/  "The OptoWire III was then reconnected to the OptoMonitor and post-PCI physiology repeated with an increase in resting dPR to 0.97, indicating no residual flow limitation. The OptoWire III was withdrawn to the tip of the guide catheter, an absence of pressure drift confirmed, and the wire and guiding catheter removed. The patient was symptom-free and in stable condition at the procedure end."  https://www.hmpgloballearningnetwork.com/site/cathlab/content/opsens-optowire-iii-next-generation-workhorse-pressure-guidewire
1[b]	A processing unit in communication with the pressure-sensing guide wire and a pressure-sensing instrument, the processing unit configured to:	Upon information and belief, the Accused Products, including at least the OptoMonitor, OptoWire, and accompanying auxiliary products, comprise A processing unit in communication with the pressure-sensing guide wire and a pressure-sensing instrument. Exemplary public evidence includes the following excerpts from OpSens' website:



cardiac cycle
of the patient,
wherein the
proximal
pressure
measurements
are obtained
without
application of a
hyperemic
agent to the
patient;

DPR	Diastolic pressure ratio	Average Pd/Pa during the entire diastole	Generic— Opsens, Acist (?)
dPR	Diastolic pressure ratio	Pd/Pa during the flat period of the dP/dt signal (the wave-free period)	Generic— Erasmus MC/ Rotterdam

See

https://www.ahajournals.org/doi/10.1161/CIRCINTERVENTIONS.118.007540.

"The OptoMonitor<sup>TM</sup> system brings a variety of solutions to help you manage all measurements directly at the table side or by integrating physiology measurements into your hemodynamic system."

	FFR	Pd/Pa	cFFR	dPR
Valeur de coupure	0.80 <sup>1</sup>	0.91 <sup>2</sup>	0.83 <sup>3</sup>	0.894
Correlation vs FFR		81.5% <sup>2</sup>	85.8% <sup>3</sup>	
Correlation vs iFR™				98%4

https://opsensmedical.com/products/optomonitor/

"dPR is a resting index which consists in calculating the ratio of Pd and Pa over the diastolic portion of the heart beat cycle. dPR is a resting index for the diagnostic of the severity of stenosis equivalent to iFR (instantaneous wave-Free Ratio).

iFR calculates the ratio of Pd and Pa over 75% of the diastolic portion. The accuracy, specificity and sensitivity of dPR compared to iFR as a reference standard1, using the same cut-off value of 0.89 and calculated from both CONTRAST2 and VERIFY 23 studies, are 97.1% [95.7%, 98.1% @95%CI], 95.9% [93.6%, 97.5% @95%CI] and 98.4 [96.6%, 99.3% @95%CI] respectively.

The diagnostic performance of dPR (cut-off=0.89) vs FFR (cut-off=0.80) compared to iFR (cut-off=0.89) vs FFR (cut-off=0.80) was also assessed. It was demonstrated that the diagnostic performance of dPR vs FFR is not statistically different from the diagnostic performance of iFR vs FFR, with 95% confidence interval significantly overlapping."

Opsens Submission for FDA Approval, see Complaint Exhibit C at p. 5.

"dPR and iFR are resting indices used for the diagnostic of the severity of stenosis with the patient in resting condition, as opposed to inducing hyperemia when measuring FFR. dPR modality consists in calculating the ratio of Pd and Pa over the whole diastolic portion of the heart beat cycle while iFR calculate the same ratio over 75% of the diastole. Performance testing has confirmed equivalence of the proposed device to iFR (reference device)."

Opsens Submission for FDA Approval, see Complaint Exhibit C at p. 7.

Receive distal pressure measurements obtained by the pressure monitoring element of the pressuresensing guide wire during the cardiac cycle of the patient, wherein the distal pressure measurements are obtained without the application of the hyperemic agent to the patient;

1[d]

Upon information and belief, the Accused Products, including at least the OptoMonitor, OptoWire, and accompanying auxiliary products, comprise a processing unit configured to receive distal pressure measurements obtained by the pressure monitoring element of the pressure-sensing guide wire during the cardiac cycle of the patient, wherein the distal pressure measurements are obtained without the application of the hyperemic agent to the patient. Exemplary public evidence includes the following excerpts from OpSens' website:

DPR	Diastolic pressure ratio	Average Pd/Pa during the entire diastole	Generic— Opsens, Acist (?)
dPR	Diastolic pressure ratio	Pd/Pa during the flat period of the dP/dt signal (the wave-free period)	Generic— Erasmus MC/ Rotterdam

See

https://www.ahajournals.org/doi/10.1161/CIRCINTERVENTIONS.118.007540.

"The OptoMonitor<sup>TM</sup> system brings a variety of solutions to help you manage all measurements directly at the table side or by integrating physiology measurements into your hemodynamic system."

With the OptoWire and OptoMonitor, you have the choice to measure different physiologic indices:						
	FFR	Pd/Pa	cFFR	dPR		
Valeur de coupure	0.80 <sup>1</sup>	0.91 <sup>2</sup>	0.83 <sup>3</sup>	0.894		
Correlation vs FFR		81.5% <sup>2</sup>	85.8% <sup>3</sup>			
Correlation vs iFR™				98%4		
1 Tonino PA et al. Fractional flow reserve versus angiography for guiding percutaneous coronary intervention. N Engl J Med 2009;360:213-24 2 Jeremias, J Am Coll Cardiol, 2014; 3 Johnson N, et al. J Am Coll Cardiol Intv 2016;9:757-67; 4 Marcel van't Veer et al. J Am Coll Cardiol. 2017 Dec 26;70(25):3088-3096. doi: 10.1016/j.jacc.2017.10.066						

https://opsensmedical.com/products/optomonitor/

"dPR is a resting index which consists in calculating the ratio of Pd and Pa over the diastolic portion of the heart beat cycle. dPR is a resting index for the

diagnostic of the severity of stenosis equivalent to iFR (instantaneous wave-Free Ratio). iFR calculates the ratio of Pd and Pa over 75% of the diastolic portion. The accuracy, specificity and sensitivity of dPR compared to iFR as a reference standard1, using the same cut-off value of 0.89 and calculated from both CONTRAST2 and VERIFY 23 studies, are 97.1% [95.7%, 98.1% @95%CI], 95.9% [93.6%, 97.5% @95%CI] and 98.4 [96.6%, 99.3% @95%CI] respectively. The diagnostic performance of dPR (cut-off=0.89) vs FFR (cut-off=0.80) compared to iFR (cut-off=0.89) vs FFR (cut-off=0.80) was also assessed. It was demonstrated that the diagnostic performance of dPR vs FFR is not statistically different from the diagnostic performance of iFR vs FFR, with 95% confidence interval significantly overlapping." Opsens Submission for FDA Approval, see Complaint Exhibit C at p. 5. "dPR and iFR are resting indices used for the diagnostic of the severity of stenosis with the patient in resting condition, as opposed to inducing hyperemia when measuring FFR. dPR modality consists in calculating the ratio of Pd and Pa over the whole diastolic portion of the heart beat cycle while iFR calculate the same ratio over 75% of the diastole. Performance testing has confirmed equivalence of the proposed device to iFR (reference device)." Opsens Submission for FDA Approval, see Complaint Exhibit C at p. 7. Select a Upon information and belief, the Accused Products, including at least the 1[e] OptoMonitor, OptoWire, and accompanying auxiliary products, comprise a diagnostic window within processing unit configured to select a diagnostic window within the cardiac cycle the cardiac of the patient, wherein a starting point of the diagnostic window is determined cycle of the based on at least one of the received proximal pressure measurements or the patient, received distal pressure measurements and an ending point of the diagnostic wherein a window is determined based on at least one of the received proximal pressure starting point measurements or the received distal pressure measurements such that the of the diagnostic window encompasses only a portion of the cardiac cycle of the patient. diagnostic Exemplary public evidence includes the following excerpts from OpSens' window is website: determined based on at

least one of the

received proximal

pressure measurements or the received distal pressure measurements and an ending point of the diagnostic window is determined based on at least one of the received proximal pressure measurements or the received distal pressure measurements such that the diagnostic window encompasses only a portion of the cardiac cycle of the patient;

dPR Diastolic pressure Pd/Pa during the flat Frasmus MC/ signal (the wave-free period)  Diastolic pressure Pd/Pa during the flat Frasmus MC/ signal (the wave-free period)	DPR	Diastolic pressure ratio	Average Pd/Pa during the entire diastole	Generic— Opsens, Acist (?)
	dPR		period of the dP/dt	Erasmus MC/

See

https://www.ahajournals.org/doi/10.1161/CIRCINTERVENTIONS.118.007540.

"The OptoMonitor<sup>TM</sup> system brings a variety of solutions to help you manage all measurements directly at the table side or by integrating physiology measurements into your hemodynamic system."

With the OptoWire and OptoMonitor, you have the choice to measure different physiologic indices:						
	FFR	Pd/Pa	cFFR	dPR		
Valeur de coupure	0.80 <sup>1</sup>	0.91 <sup>2</sup>	0.83 <sup>3</sup>	0.894		
Correlation vs FFR		81.5% <sup>2</sup>	85.8% <sup>3</sup>			
Correlation vs iFR™				98%4		
1 Tonino PA et al. Fractional flow reserve versus angiography for guiding percutaneous coronary intervention. N Engl J Med 2009;360:213-24 2 Jeremias, J Am Coll Cardiol, 2014; 3 Johnson N, et al. J Am Coll Cardiol Intv 2016;9:757-67; 4 Marcel van't Veer et al. J Am Coll Cardiol. 2017 Dec 26;70(25):3088-3096. doi: 10.1016/j.jacc.2017.10.066						

https://opsensmedical.com/products/optomonitor/

"dPR is a resting index which consists in calculating the ratio of Pd and Pa over the diastolic portion of the heart beat cycle. dPR is a resting index for the diagnostic of the severity of stenosis equivalent to iFR (instantaneous wave-Free Ratio).

iFR calculates the ratio of Pd and Pa over 75% of the diastolic portion. The accuracy, specificity and sensitivity of dPR compared to iFR as a reference standard1, using the same cut-off value of 0.89 and calculated from both CONTRAST2 and VERIFY 23 studies, are 97.1% [95.7%, 98.1% @95%CI], 95.9% [93.6%, 97.5% @95%CI] and 98.4 [96.6%, 99.3% @95%CI] respectively.

The diagnostic performance of dPR (cut-off=0.89) vs FFR (cut-off=0.80) compared to iFR (cut-off=0.89) vs FFR (cut-off=0.80) was also assessed. It was demonstrated that the diagnostic performance of dPR vs FFR is not statistically different from the diagnostic performance of iFR vs FFR, with 95% confidence interval significantly overlapping."

Opsens Submission for FDA Approval, see Complaint Exhibit C at p. 5.

"dPR and iFR are resting indices used for the diagnostic of the severity of stenosis with the patient in resting condition, as opposed to inducing hyperemia when measuring FFR. dPR modality consists in calculating the ratio of Pd and Pa over the whole diastolic portion of the heart beat cycle while iFR calculate the same ratio over 75% of the diastole. Performance testing has confirmed equivalence of the proposed device to iFR (reference device)."

*Opsens Submission for FDA Approval, see* Complaint Exhibit C at p. 7.

1[f] pressure ratio based on a plurality of distal pressure measurements obtained during the diagnostic window and a plurality of proximal pressure measurements

> obtained during the diagnostic window; and

Calculate a

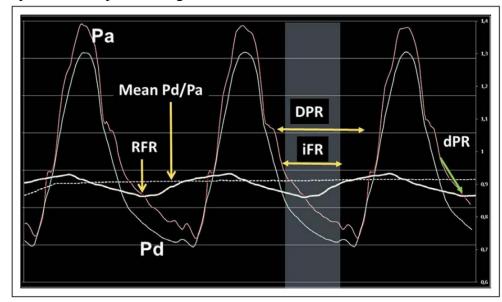
Upon information and belief, the Accused Products, including at least the OptoMonitor, OptoWire, and accompanying auxiliary products, comprise a processing unit configured to calculate a pressure ratio based on a plurality of distal pressure measurements obtained during the diagnostic window and a plurality of proximal pressure measurements obtained during the diagnostic window. Exemplary public evidence includes the following excerpts from OpSens' website:



https://opsensmedical.com/products/optomonitor/

DPR	Diastolic pressure ratio	Average Pd/Pa during the entire diastole	Generic— Opsens, Acist (?)
dPR	Diastolic pressure ratio	Pd/Pa during the flat period of the dP/dt signal (the wave-free period)	Generic— Erasmus MC/ Rotterdam

*See* https://www.ahajournals.org/doi/10.1161/CIRCINTERVENTIONS.118.007540.



See https://www.ahajournals.org/doi/10.1161/CIRCINTERVENTIONS.118.007540 (annotation in original).

"dPR is a resting index which consists in calculating the ratio of Pd and Pa over the diastolic portion of the heart beat cycle. dPR is a resting index for the diagnostic of the severity of stenosis equivalent to iFR (instantaneous wave-Free Ratio).

iFR calculates the ratio of Pd and Pa over 75% of the diastolic portion. The accuracy, specificity and sensitivity of dPR compared to iFR as a reference standard1, using the same cut-off value of 0.89 and calculated from both CONTRAST2 and VERIFY 23 studies, are 97.1% [95.7%, 98.1% @95%CI], 95.9% [93.6%, 97.5% @95%CI] and 98.4 [96.6%, 99.3% @95%CI] respectively.

The diagnostic performance of dPR (cut-off=0.89) vs FFR (cut-off=0.80) compared to iFR (cut-off=0.89) vs FFR (cut-off=0.80) was also assessed. It was demonstrated that the diagnostic performance of dPR vs FFR is not statistically different from the diagnostic performance of iFR vs FFR, with 95% confidence interval significantly overlapping."

Opsens Submission for FDA Approval, see Complaint Exhibit C at p. 6.

"dPR and iFR are resting indices used for the diagnostic of the severity of stenosis with the patient in resting condition, as opposed to inducing hyperemia when measuring FFR. dPR modality consists in calculating the ratio of Pd and Pa over

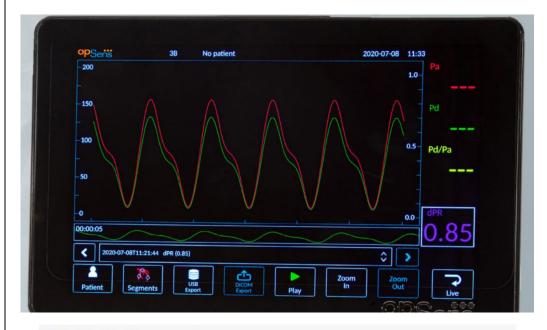
the whole diastolic portion of the heart beat cycle while iFR calculate the same ratio over 75% of the diastole. Performance testing has confirmed equivalence of the proposed device to iFR (reference device)."

Opsens Submission for FDA Approval, see Complaint Exhibit C at p. 7.

1[g] Output, to a display in communication with the processing unit, the calculated pressure ratio for evaluating the stenosis of the vessel without a hyperemic physiological effect on the

patent,

Upon information and belief, the Accused Products, including at least the OptoMonitor, OptoWire, and accompanying auxiliary products, comprise a processing unit configured to output, to a display in communication with the processing unit, the calculated pressure ratio for evaluating the stenosis of the vessel without a hyperemic physiological effect on the patent. Exemplary public evidence includes the following excerpts from OpSens' website:





https://opsensmedical.com/products/optomonitor/

DPR	Diastolic pressure ratio	Average Pd/Pa during the entire diastole	Generic— Opsens, Acist (?)
dPR	Diastolic pressure ratio	Pd/Pa during the flat period of the dP/dt signal (the wave-free period)	Generic— Erasmus MC/ Rotterdam

https://www.ahajournals.org/doi/10.1161/CIRCINTERVENTIONS.118.007540.

pressure ratio
is calculated as
an average of
the plurality of
distal pressure

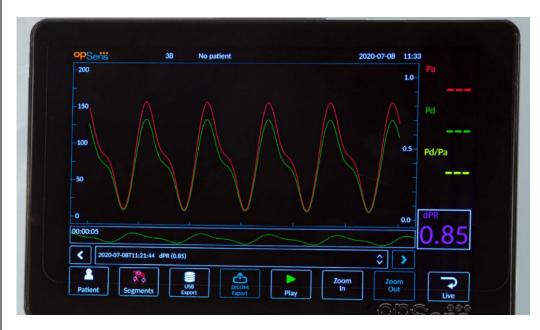
1[h]

an average of the plurality of distal pressure measurements obtained during the diagnostic window divided by an average of the plurality of proximal pressure measurements obtained

during the diagnostic window.

Wherein the

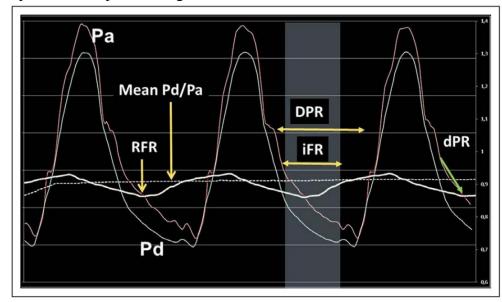
Upon information and belief, the Accused Products, including at least the OptoMonitor, OptoWire, and accompanying auxiliary products, calculate a pressure ratio as an average of the plurality of distal pressure measurements obtained during the diagnostic window divided by an average of the plurality of proximal pressure measurements obtained during the diagnostic window. Exemplary public evidence includes the following excerpts from OpSens' website:



https://opsensmedical.com/products/optomonitor/

DPR	Diastolic pressure ratio	Average Pd/Pa during the entire diastole	Generic— Opsens, Acist (?)
dPR	Diastolic pressure ratio	Pd/Pa during the flat period of the dP/dt signal (the wave-free period)	Generic— Erasmus MC/ Rotterdam

*See* https://www.ahajournals.org/doi/10.1161/CIRCINTERVENTIONS.118.007540.



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"dPR is a resting index which consists in calculating the ratio of Pd and Pa over the diastolic portion of the heart beat cycle. dPR is a resting index for the diagnostic of the severity of stenosis equivalent to iFR (instantaneous wave-Free Ratio).

iFR calculates the ratio of Pd and Pa over 75% of the diastolic portion. The accuracy, specificity and sensitivity of dPR compared to iFR as a reference standard1, using the same cut-off value of 0.89 and calculated from both CONTRAST2 and VERIFY 23 studies, are 97.1% [95.7%, 98.1% @95%CI], 95.9% [93.6%, 97.5% @95%CI] and 98.4 [96.6%, 99.3% @95%CI] respectively.

The diagnostic performance of dPR (cut-off=0.89) vs FFR (cut-off=0.80) compared to iFR (cut-off=0.89) vs FFR (cut-off=0.80) was also assessed. It was demonstrated that the diagnostic performance of dPR vs FFR is not statistically different from the diagnostic performance of iFR vs FFR, with 95% confidence interval significantly overlapping."

Opsens Submission for FDA Approval, see Complaint Exhibit C at p. 6.

"dPR and iFR are resting indices used for the diagnostic of the severity of stenosis with the patient in resting condition, as opposed to inducing hyperemia when measuring FFR. dPR modality consists in calculating the ratio of Pd and Pa over

	the whole diastolic portion of the heart beat cycle while iFR calculate the same ratio over 75% of the diastole. Performance testing has confirmed equivalence of the proposed device to iFR (reference device)."
	Opsens Submission for FDA Approval, see Complaint Exhibit C at p. 7.

11[pre]	A system for evaluating a stenosis of a vessel, the system comprising:	Upon information and be OptoMonitor, OptoWire system for evaluating as includes the following of the OpSens OptoWire is guidewire designed avessels such as corological optoWire is powered 2nd generation fiber measure physiological Fractional Flow Research Pressure Ratio (dPR)  MORE INFORMATION  https://opsensmedical.com/	e, and accompany seessing a stenosic excerpts from Option a modern present of assess stenosic excerpts from Optionary arteries.  If by Fidela <sup>™</sup> , a optic sensor to eximple the including erve (FFR and described of the including erve (FFR and d	ying auxiliar s of a vessel Sens' websit sure oses in patented ng liastolic	y products, co . Exemplary p re:	omprise a public evidence	
		physiologic indices:					
			FFR	Pd/Pa	cFFR	dPR	
		Valeur de coupure	0.80 <sup>1</sup>	0.91 <sup>2</sup>	0.83 <sup>3</sup>	0.894	
		Correlation vs FFR		81.5% <sup>2</sup>	85.8% <sup>3</sup>	200/4	
		Correlation vs iFR™				98%4	
		1 Tonino PA et al. Fractional flow reserve versu Cardiol, 2014; 3 Johnson N, et al. J Am Coll Card 10.1016/j.jacc.2017.10.066	is angiography for guiding percutai diol Intv 2016;9:757–67; 4 Marcel				
		https://opsensmedical.co	-	omonitor/			
		"5.6 INDICATIONS FOR USE					
		To measure pressure in vessels, during diagnost Blood pressure measure fractional flow reserve, <i>OpSens Submission for</i>	ic angiography a ments provide he for the diagnosis	nd/or any in emodynamic and treatme	terventional p information, nt of blood ve	orocedures. such as essel disease."	
11[a]	a pressure- sensing guide wire sized and	Upon information and b OptoMonitor, OptoWire pressure-sensing guide	e, and accompany	ying auxiliar	y products, co	omprise a	

shaped for introduction into the vessel of the patient, the pressuresensing guide wire comprising a proximal portion, a distal portion, and a pressuremonitoring element coupled to the distal portion;

the patient, the pressure-sensing guide wire comprising a proximal portion, a distal portion, and a pressure-monitoring element coupled to the distal portion. Exemplary public evidence includes:



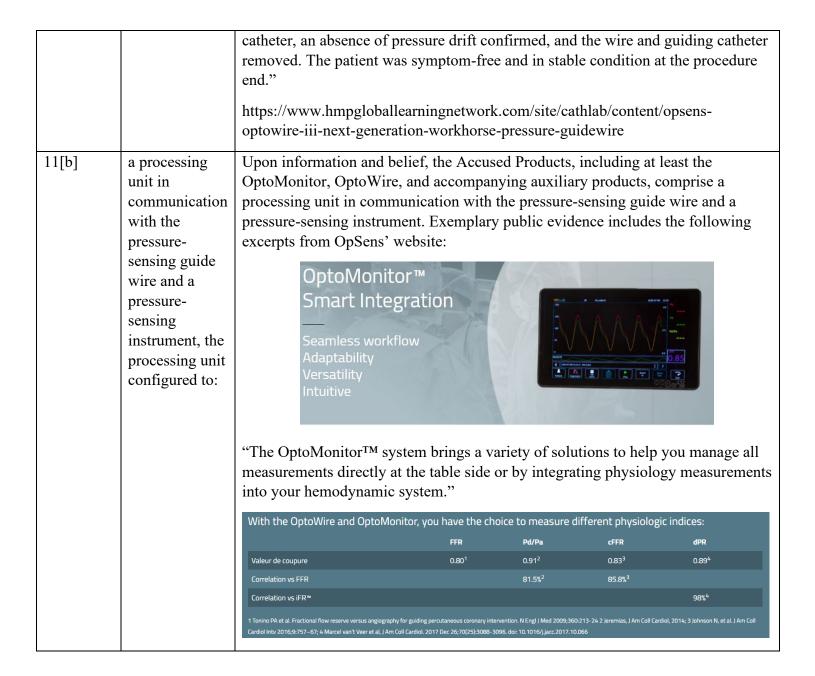
"OptoWire

OpSens OptoWire is a modern pressure guidewire designed to assess stenoses in vessels such as coronary arteries."



https://opsensmedical.com/products/optowire/

"The OptoWire III was then reconnected to the OptoMonitor and post-PCI physiology repeated with an increase in resting dPR to 0.97, indicating no residual flow limitation. The OptoWire III was withdrawn to the tip of the guide





https://opsensmedical.com/products/optomonitor/

receive proximal pressure measurements and distal pressure measurements, wherein the proximal and distal pressure measurements are respectively obtained by the pressuresensing instrument and the pressuresensing guide wire without application of a hyperemic agent to the

patient;

11[c]

Upon information and belief, the Accused Products, including at least the OptoMonitor, OptoWire, and accompanying auxiliary products, comprise a processing unit configured to receive proximal pressure measurements and distal pressure measurements, wherein the proximal and distal pressure measurements are respectively obtained by the pressure-sensing instrument and the pressure-sensing guide wire without application of a hyperemic agent to the patient. Exemplary public evidence includes:

DPR	Diastolic pressure ratio	Average Pd/Pa during the entire diastole	Generic— Opsens, Acist (?)
dPR	Diastolic pressure ratio	Pd/Pa during the flat period of the dP/dt signal (the wave-free period)	Generic— Erasmus MC/ Rotterdam

See

https://www.ahajournals.org/doi/10.1161/CIRCINTERVENTIONS.118.007540.

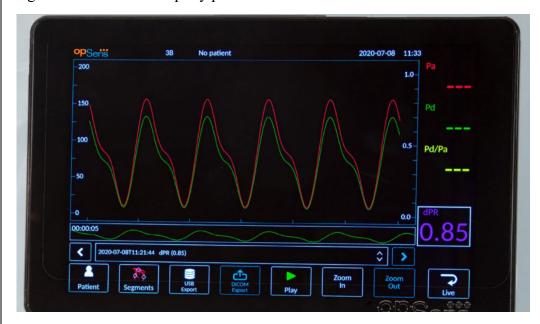
"The OptoMonitor<sup>TM</sup> system brings a variety of solutions to help you manage all measurements directly at the table side or by integrating physiology measurements into your hemodynamic system."

	FFR	Pd/Pa	cFFR	dPR
aleur de coupure	0.80 <sup>1</sup>	0.91 <sup>2</sup>	0.83 <sup>3</sup>	0.894
Correlation vs FFR		81.5% <sup>2</sup>	85.8% <sup>3</sup>	
orrelation vs iFR™				98%4

https://opsensmedical.com/products/optomonitor/ "dPR is a resting index which consists in calculating the ratio of Pd and Pa over the diastolic portion of the heart beat cycle. dPR is a resting index for the diagnostic of the severity of stenosis equivalent to iFR (instantaneous wave-Free Ratio). iFR calculates the ratio of Pd and Pa over 75% of the diastolic portion. The accuracy, specificity and sensitivity of dPR compared to iFR as a reference standard1, using the same cut-off value of 0.89 and calculated from both CONTRAST2 and VERIFY 23 studies, are 97.1% [95.7%, 98.1% @95%CI], 95.9% [93.6%, 97.5% @95%CI] and 98.4 [96.6%, 99.3% @95%CI] respectively. The diagnostic performance of dPR (cut-off=0.89) vs FFR (cut-off=0.80) compared to iFR (cut-off=0.89) vs FFR (cut-off=0.80) was also assessed. It was demonstrated that the diagnostic performance of dPR vs FFR is not statistically different from the diagnostic performance of iFR vs FFR, with 95% confidence interval significantly overlapping." Opsens Submission for FDA Approval, see Complaint Exhibit C at p. 5. "dPR and iFR are resting indices used for the diagnostic of the severity of stenosis with the patient in resting condition, as opposed to inducing hyperemia when measuring FFR. dPR modality consists in calculating the ratio of Pd and Pa over the whole diastolic portion of the heart beat cycle while iFR calculate the same ratio over 75% of the diastole. Performance testing has confirmed equivalence of the proposed device to iFR (reference device)." *Opsens Submission for FDA Approval, see* Complaint Exhibit C at p. 7. 11[d] Upon information and belief, the Accused Products, including at least the calculate a OptoMonitor, OptoWire, and accompanying auxiliary products, comprise a pressure ratio for a diagnostic processing unit configured to calculate a pressure ratio for a diagnostic window of window of a a cardiac cycle of the patient, wherein a starting point of the diagnostic window is cardiac cycle determined based on at least one of the received proximal pressure measurements of the patient, or the received distal pressure measurements and an ending point of the diagnostic wherein a window is determined based on at least one of the received proximal pressure measurements or the received distal pressure measurements such that the starting point of the diagnostic window encompasses only a portion of the cardiac cycle of the patient, diagnostic wherein the pressure ratio is calculated as an average of the received distal window is pressure measurements obtained during the diagnostic window divided by an determined based on at

least one of the received proximal pressure measurements or the received distal pressure measurements and an ending point of the diagnostic window is determined based on at least one of the received proximal pressure measurements or the received distal pressure measurements such that the diagnostic window encompasses only a portion of the cardiac cycle of the patient, wherein the pressure ratio is calculated as an average of the received distal pressure measurements obtained during the diagnostic window divided by an average of the

average of the received proximal pressure measurements obtained during the diagnostic window. Exemplary public evidence includes:

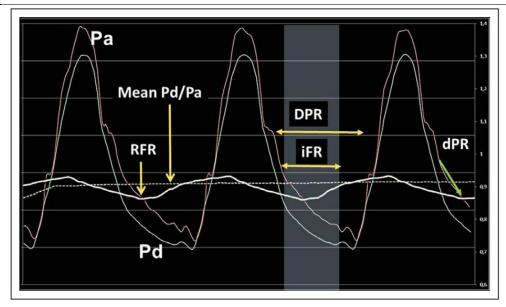


https://opsensmedical.com/products/optomonitor/

DPR	Diastolic pressure ratio	Average Pd/Pa during the entire diastole	Generic— Opsens, Acist (?)
dPR	Diastolic pressure ratio	Pd/Pa during the flat period of the dP/dt signal (the wave-free period)	Generic— Erasmus MC/ Rotterdam

See https://www.ahajournals.org/doi/10.1161/CIRCINTERVENTIONS.118.007540.

received proximal pressure measurements obtained during the diagnostic window; and



See https://www.ahajournals.org/doi/10.1161/CIRCINTERVENTIONS.118.007540 (annotation in original).

"dPR is a resting index which consists in calculating the ratio of Pd and Pa over the diastolic portion of the heart beat cycle. dPR is a resting index for the diagnostic of the severity of stenosis equivalent to iFR (instantaneous wave-Free Ratio).

iFR calculates the ratio of Pd and Pa over 75% of the diastolic portion. The accuracy, specificity and sensitivity of dPR compared to iFR as a reference standard1, using the same cut-off value of 0.89 and calculated from both CONTRAST2 and VERIFY 23 studies, are 97.1% [95.7%, 98.1% @95%CI], 95.9% [93.6%, 97.5% @95%CI] and 98.4 [96.6%, 99.3% @95%CI] respectively.

The diagnostic performance of dPR (cut-off=0.89) vs FFR (cut-off=0.80) compared to iFR (cut-off=0.89) vs FFR (cut-off=0.80) was also assessed. It was demonstrated that the diagnostic performance of dPR vs FFR is not statistically different from the diagnostic performance of iFR vs FFR, with 95% confidence interval significantly overlapping."

Opsens Submission for FDA Approval, see Complaint Exhibit C at p. 6.

"dPR and iFR are resting indices used for the diagnostic of the severity of stenosis with the patient in resting condition, as opposed to inducing hyperemia when measuring FFR. dPR modality consists in calculating the ratio of Pd and Pa over the whole diastolic portion of the heart beat cycle while iFR calculate the same

ratio over 75% of the diastole. Performance testing has confirmed equivalence of

the proposed device to iFR (reference device)." Opsens Submission for FDA Approval, see Complaint Exhibit C at p. 7. Upon information and belief, the Accused Products, including at least the 11[e] output, to a display in OptoMonitor, OptoWire, and accompanying auxiliary products, comprise a communication processing unit configured to output, to a display in communication with the with the processing unit, the calculated pressure ratio for evaluating the stenosis of the processing vessel without a hyperemic physiological effect on the patient. Exemplary public unit, the evidence includes: calculated pressure ratio for evaluating No patient 2020-07-08 the stenosis of the vessel 150 without a hyperemic Pd/Pa physiological effect on the patient. 2020-07-08T11:21:44 dPR (0.85) OptoMonitor Components: OptoMonitor 10" Display Compute and display hemodynamics data

Optical Box

https://opsensmedical.com/products/optomonitor/

Send/receive light to/from OptoWire

Handle Unit

Connect OptoWire with Optical Box

## 

		DPR	Diastolic pressure ratio	Average Pd/Pa during the entire diastole	Generic— Opsens, Acist (?)	
		dPR	Diastolic pressure ratio	Pd/Pa during the flat period of the dP/dt signal (the wave-free period)	Generic— Erasmus MC/ Rotterdam	
h	ttps://ww	ww.ahajo	urnals.org/doi/10.1	161/CIRCINTERVE	NTIONS.118.00	7540.

26[pre]	A system for evaluating a stenosis of a vessel of a patient, the system comprising:	Upon information and OptoMonitor, OptoWirs system for evaluating a evidence includes the formation opposed optoWire is guidewire designed vessels such as corresponding to the control optoWire is powered and generation fiber measure physiological Fractional Flow Responding Pressure Ratio (dPF) MORE INFORMATION	re, and accompany a stenosis of a vest collowing excerpts a modern present to assess stend on ary arteries. Red by Fidela <sup>™</sup> , a roptic sensor to cindices including ferve (FFR and configuration).	ying auxiliar, sel of a patie is from OpSer is sure oses in patented ing diastolic owire/	y products, cont. Exemplary	omprise a y public		
		With the OptoWire and ophysiologic indices:	OptoMonitor, you h	ave the choice	e to measure d	lifferent		
			FFR	Pd/Pa	cFFR	dPR		
		Valeur de coupure	0.80 <sup>1</sup>	0.91 <sup>2</sup>	0.83 <sup>3</sup>	0.894		
		Correlation vs FFR		81.5% <sup>2</sup>	85.8% <sup>3</sup>			
		Correlation vs iFR™				98%4		
		1 Tonino PA et al. Fractional flow reserve ver Cardiol, 2014; 3 Johnson N, et al. J Am Coll Ca 10.1016/j.jacc.2017.10.066						
		https://opsensmedical.co	com/products/opto	omonitor/				
		"5.6 INDICATIONS FOR USE						
		To measure pressure in vessels, during diagnos Blood pressure measur fractional flow reserve.	stic angiography a rements provide he for the diagnosis	and/or any intermediates and treatme	terventional prinformation, nt of blood ve	orocedures. such as essel disease."		
		OpSens Submission for	· FDA Approval, (	Complaint Ex	xhibit C, p. 5.			
26[a]	A pressure- sensing guide wire sized and	Upon information and OptoMonitor, OptoWin pressure-sensing guide	re, and accompany	ying auxiliar	y products, co	omprise A		

shaped for introduction into the vessel of the patient, the pressuresensing guide wire comprising a proximal portion, a distal portion, and a pressure monitoring element coupled to the distal portion;

the patient, the pressure-sensing guide wire comprising a proximal portion, a distal portion, and a pressure monitoring element coupled to the distal portion. Exemplary public evidence includes the following excerpts from OpSens' website:



"OptoWire

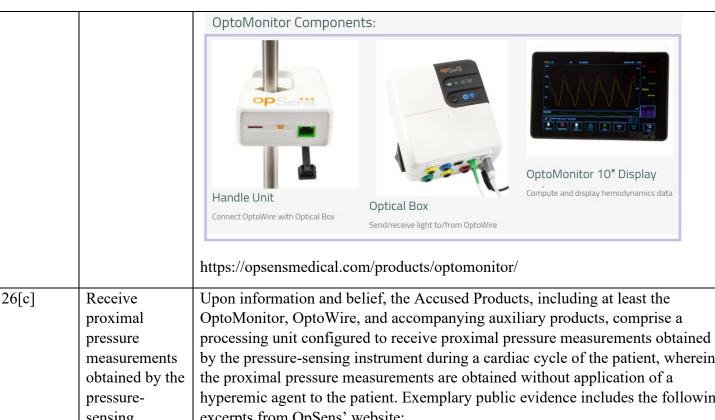
OpSens OptoWire is a modern pressure guidewire designed to assess stenoses in vessels such as coronary arteries."



https://opsensmedical.com/products/optowire/

"The OptoWire III was then reconnected to the OptoMonitor and post-PCI physiology repeated with an increase in resting dPR to 0.97, indicating no residual

flow limitation. The OptoWire III was withdrawn to the tip of the guide catheter, an absence of pressure drift confirmed, and the wire and guiding catheter removed. The patient was symptom-free and in stable condition at the procedure end." https://www.hmpgloballearningnetwork.com/site/cathlab/content/opsensoptowire-iii-next-generation-workhorse-pressure-guidewire 26[b] A processing Upon information and belief, the Accused Products, including at least the unit in OptoMonitor, OptoWire, and accompanying auxiliary products, comprise A communication processing unit in communication with the pressure-sensing guide wire and a with the pressure-sensing instrument. Exemplary public evidence includes the following excerpts from OpSens' website: pressuresensing guide OptoMonitor™ wire and a Smart Integration pressuresensing instrument, the Seamless workflow processing unit configured to: "The OptoMonitor<sup>TM</sup> system brings a variety of solutions to help you manage all measurements directly at the table side or by integrating physiology measurements into your hemodynamic system." With the OptoWire and OptoMonitor, you have the choice to measure different physiologic indices: cFFR Pd/Pa 0.91<sup>2</sup> 0.83<sup>3</sup> Valeur de coupure Correlation vs FFR 98%4 . Fractional flow reserve versus angiography for guiding percutaneous coronary intervention. N Engl J Med 2009;360:213-24 2 Jeremias, J Am Coll Cardiol, 2014; 3 Johnson N, et al. J Am Coll 5;9-757-67; 4 Marcel van't Veer et al, J Am Coll Cardiol. 2017 Dec 26;70(25):3088-3096. doi: 10.1016/j.jacc.2017.10.066



sensing instrument during a cardiac cycle of the patient, wherein the proximal pressure measurements are obtained without application of a hyperemic agent to the patient;

by the pressure-sensing instrument during a cardiac cycle of the patient, wherein hyperemic agent to the patient. Exemplary public evidence includes the following excerpts from OpSens' website:

DPR	Diastolic pressure ratio	Average Pd/Pa during the entire diastole	Generic— Opsens, Acist (?)
dPR	Diastolic pressure ratio	Pd/Pa during the flat period of the dP/dt signal (the wave-free period)	Generic— Erasmus MC/ Rotterdam

See

https://www.ahajournals.org/doi/10.1161/CIRCINTERVENTIONS.118.007540.

"The OptoMonitor<sup>TM</sup> system brings a variety of solutions to help you manage all measurements directly at the table side or by integrating physiology measurements into your hemodynamic system."

		With the OptoWire and OptoMonitor, yo	u have the choic	ce to me <u>asure d</u>	ifferent physiologi	c indices:
			FFR	Pd/Pa	cFFR	dPR
		Valeur de coupure	0.80 <sup>1</sup>	0.91 <sup>2</sup>	0.83 <sup>3</sup>	0.894
		Correlation vs FFR		81.5% <sup>2</sup>	85.8% <sup>3</sup>	
		Correlation vs iFR™				98%4
		1 Tonino PA et al. Fractional flow reserve versus angiography for guiding p Cardiol Intv 2016;9:757–67; 4 Marcel van't Veer et al, J Am Coll Cardiol. 20				liol, 2014; 3 Johnson N, et al. J Am Coll
		https://opsensmedical.com/pro	oducts/opto	monitor/		
		"dPR is a resting index which consists in calculating the ratio of Pd and Pa over the diastolic portion of the heart beat cycle. dPR is a resting index for the diagnostic of the severity of stenosis equivalent to iFR (instantaneous wave-Free Ratio).				
		iFR calculates the ratio of Pd accuracy, specificity and sens standard1, using the same cur CONTRAST2 and VERIFY 2 95.9% [93.6%, 97.5% @95%	itivity of dF t-off value of tage of the state of the sta	PR compare of 0.89 and are 97.1% [9	d to iFR as a calculated fro 95.7%, 98.1%	reference om both o @95%CI],
		The diagnostic performance of dPR (cut-off=0.89) vs FFR (cut-off=0.80) compared to iFR (cut-off=0.89) vs FFR (cut-off=0.80) was also assessed. It was demonstrated that the diagnostic performance of dPR vs FFR is not statistically different from the diagnostic performance of iFR vs FFR, with 95% confidence interval significantly overlapping."				
		Opsens Submission for FDA	Approval, se	ee Complair	nt Exhibit C a	at p. 5.
		"dPR and iFR are resting indiwith the patient in resting commeasuring FFR. dPR modality the whole diastolic portion of ratio over 75% of the diastole the proposed device to iFR (restaurant of the proposed device)."	dition, as og y consists in the heart be . Performan	pposed to in a calculating eat cycle whate testing h	nducing hyper g the ratio of nile iFR calcu	remia when Pd and Pa over llate the same
		Opsens Submission for FDA 2	Approval, se	ee Complain	nt Exhibit C a	nt p. 7.
26[d]	Receive distal pressure measurements obtained by the pressure monitoring	Upon information and belief, OptoMonitor, OptoWire, and processing unit configured to the pressure monitoring eleme cardiac cycle of the patient, w	accompany receive dist ent of the pr	ing auxiliant al pressure ressure-sens	ry products, c measurement sing guide win	omprise a ts obtained by re during the

element of the pressuresensing guide wire during the cardiac cycle of the patient, wherein the distal pressure measurements are obtained without the application of the hyperemic patient to the patient;

without the application of the hyperemic patient to the patient. Exemplary public evidence includes the following excerpts from OpSens' website:

DPR	Diastolic pressure ratio	Average Pd/Pa during the entire diastole	Generic— Opsens, Acist (?)
dPR	Diastolic pressure ratio	Pd/Pa during the flat period of the dP/dt signal (the wave-free period)	Generic— Erasmus MC/ Rotterdam

See

https://www.ahajournals.org/doi/10.1161/CIRCINTERVENTIONS.118.007540.

"The OptoMonitor<sup>TM</sup> system brings a variety of solutions to help you manage all measurements directly at the table side or by integrating physiology measurements into your hemodynamic system."

	FFR	Pd/Pa	cFFR	dPR
Valeur de coupure	0.80 <sup>1</sup>	0.91 <sup>2</sup>	0.83 <sup>3</sup>	0.894
Correlation vs FFR		81.5% <sup>2</sup>	85.8% <sup>3</sup>	
Correlation vs iFR™				98%4

https://opsensmedical.com/products/optomonitor/

"dPR is a resting index which consists in calculating the ratio of Pd and Pa over the diastolic portion of the heart beat cycle. dPR is a resting index for the diagnostic of the severity of stenosis equivalent to iFR (instantaneous wave-Free Ratio).

iFR calculates the ratio of Pd and Pa over 75% of the diastolic portion. The accuracy, specificity and sensitivity of dPR compared to iFR as a reference standard1, using the same cut-off value of 0.89 and calculated from both CONTRAST2 and VERIFY 23 studies, are 97.1% [95.7%, 98.1% @95%CI], 95.9% [93.6%, 97.5% @95%CI] and 98.4 [96.6%, 99.3% @95%CI] respectively.

The diagnostic performance of dPR (cut-off=0.89) vs FFR (cut-off=0.80) compared to iFR (cut-off=0.89) vs FFR (cut-off=0.80) was also assessed. It was demonstrated that the diagnostic performance of dPR vs FFR is not statistically different from the diagnostic performance of iFR vs FFR, with 95% confidence interval significantly overlapping."

*Opsens Submission for FDA Approval, see* Complaint Exhibit C at p. 5.

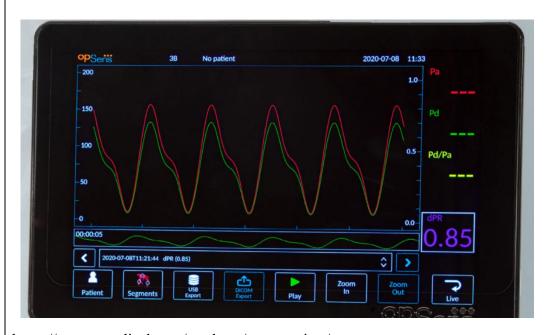
"dPR and iFR are resting indices used for the diagnostic of the severity of stenosis with the patient in resting condition, as opposed to inducing hyperemia when measuring FFR. dPR modality consists in calculating the ratio of Pd and Pa over the whole diastolic portion of the heart beat cycle while iFR calculate the same ratio over 75% of the diastole. Performance testing has confirmed equivalence of the proposed device to iFR (reference device)."

Opsens Submission for FDA Approval, see Complaint Exhibit C at p. 7.

26[e]

Select a diagnostic window within the cardiac cycle of the patient such that the diagnostic window encompasses only a portion of the cardiac cycle of the patient;

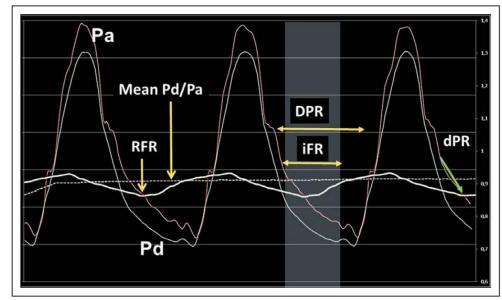
Upon information and belief, the Accused Products, including at least the OptoMonitor, OptoWire, and accompanying auxiliary products, comprise a processing unit configured to select a diagnostic window within the cardiac cycle of the patient such that the diagnostic window encompasses only a portion of the cardiac cycle of the patient. Exemplary public evidence includes the following excerpts from OpSens' website:



https://opsensmedical.com/products/optomonitor/

DPR	Diastolic pressure ratio	Average Pd/Pa during the entire diastole	Generic— Opsens, Acist (?)
dPR	Diastolic pressure ratio	Pd/Pa during the flat period of the dP/dt signal (the wave-free period)	Generic— Erasmus MC/ Rotterdam

See https://www.ahajournals.org/doi/10.1161/CIRCINTERVENTIONS.118.007540.



https://www.ahajournals.org/doi/10.1161/CIRCINTERVENTIONS.118.007540 (annotation in original).

"dPR is a resting index which consists in calculating the ratio of Pd and Pa over the diastolic portion of the heart beat cycle. dPR is a resting index for the diagnostic of the severity of stenosis equivalent to iFR (instantaneous wave-Free Ratio).

iFR calculates the ratio of Pd and Pa over 75% of the diastolic portion. The accuracy, specificity and sensitivity of dPR compared to iFR as a reference standard1, using the same cut-off value of 0.89 and calculated from both CONTRAST2 and VERIFY 23 studies, are 97.1% [95.7%, 98.1% @95%CI], 95.9% [93.6%, 97.5% @95%CI] and 98.4 [96.6%, 99.3% @95%CI] respectively.

The diagnostic performance of dPR (cut-off=0.89) vs FFR (cut-off=0.80) compared to iFR (cut-off=0.89) vs FFR (cut-off=0.80) was also assessed. It was demonstrated that the diagnostic performance of dPR vs FFR is not statistically

different from the diagnostic performance of iFR vs FFR, with 95% confidence interval significantly overlapping."

Opsens Submission for FDA Approval, see Complaint Exhibit C at p. 6.

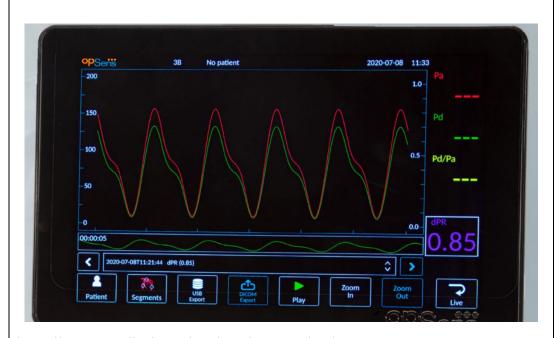
"dPR and iFR are resting indices used for the diagnostic of the severity of stenosis with the patient in resting condition, as opposed to inducing hyperemia when measuring FFR. dPR modality consists in calculating the ratio of Pd and Pa over the whole diastolic portion of the heart beat cycle while iFR calculate the same ratio over 75% of the diastole. Performance testing has confirmed equivalence of the proposed device to iFR (reference device)."

Opsens Submission for FDA Approval, see Complaint Exhibit C at p. 7.

26[f]

Calculate a pressure ratio based on a plurality of distal pressure measurements obtained during the diagnostic window and a plurality of proximal pressure measurements obtained during the diagnostic window, wherein the pressure ratio is calculated as an average of the plurality of distal pressure measurements obtained during the diagnostic window

Upon information and belief, the Accused Products, including at least the OptoMonitor, OptoWire, and accompanying auxiliary products, comprise a processing unit configured to calculate a pressure ratio based on a plurality of distal pressure measurements obtained during the diagnostic window and a plurality of proximal pressure measurements obtained during the diagnostic window, wherein the pressure ratio is calculated as an average of the plurality of distal pressure measurements obtained during the diagnostic window divided by an average of the plurality of proximal pressure measurements obtained during the diagnostic window. Exemplary public evidence includes the following excerpts from OpSens' website:



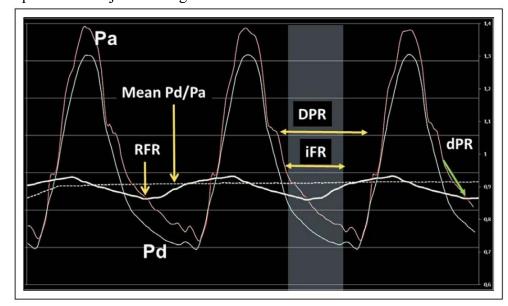
https://opsensmedical.com/products/optomonitor/

divided by an average of the plurality of proximal pressure measurements obtained during the diagnostic window; and

DPF	?	Diastolic pressure ratio	Average Pd/Pa during the entire diastole	Generic— Opsens, Acist (?)
dPF	}	Diastolic pressure ratio	Pd/Pa during the flat period of the dP/dt signal (the wave-free period)	Generic— Erasmus MC/ Rotterdam

See

https://www.ahajournals.org/doi/10.1161/CIRCINTERVENTIONS.118.007540.



See

https://www.ahajournals.org/doi/10.1161/CIRCINTERVENTIONS.118.007540 (annotation in original).

"dPR is a resting index which consists in calculating the ratio of Pd and Pa over the diastolic portion of the heart beat cycle. dPR is a resting index for the diagnostic of the severity of stenosis equivalent to iFR (instantaneous wave-Free Ratio).

iFR calculates the ratio of Pd and Pa over 75% of the diastolic portion. The accuracy, specificity and sensitivity of dPR compared to iFR as a reference standard1, using the same cut-off value of 0.89 and calculated from both CONTRAST2 and VERIFY 23 studies, are 97.1% [95.7%, 98.1% @95%CI], 95.9% [93.6%, 97.5% @95%CI] and 98.4 [96.6%, 99.3% @95%CI] respectively.

The diagnostic performance of dPR (cut-off=0.89) vs FFR (cut-off=0.80) compared to iFR (cut-off=0.89) vs FFR (cut-off=0.80) was also assessed. It was demonstrated that the diagnostic performance of dPR vs FFR is not statistically

different from the diagnostic performance of iFR vs FFR, with 95% confidence interval significantly overlapping."

Opsens Submission for FDA Approval, see Complaint Exhibit C at p. 6.

"dPR and iFR are resting indices used for the diagnostic of the severity of stenosis with the patient in resting condition, as opposed to inducing hyperemia when measuring FFR. dPR modality consists in calculating the ratio of Pd and Pa over the whole diastolic portion of the heart beat cycle while iFR calculate the same ratio over 75% of the diastole. Performance testing has confirmed equivalence of the proposed device to iFR (reference device)."

Opsens Submission for FDA Approval, see Complaint Exhibit C at p. 7.

26[g]

Output, to a display in communication with the processing unit, the calculated pressure ratio for evaluating the stenosis of the vessel without a hyperemic physiological effect on the patient.

Upon information and belief, the Accused Products, including at least the OptoMonitor, OptoWire, and accompanying auxiliary products, comprise a processing unit configured to output, to a display in communication with the processing unit, the calculated pressure ratio for evaluating the stenosis of the vessel without a hyperemic physiological effect on the patient. Exemplary public evidence includes the following excerpts from OpSens' website:





#### https://opsensmedical.com/products/optomonitor/

DPR	Diastolic pressure ratio	Average Pd/Pa during the entire diastole	Generic— Opsens, Acist (?)
dPR	Diastolic pressure ratio	Pd/Pa during the flat period of the dP/dt signal (the wave-free period)	Generic— Erasmus MC/ Rotterdam

https://www.ahajournals.org/doi/10.1161/CIRCINTERVENTIONS.118.007540.

"dPR is a resting index which consists in calculating the ratio of Pd and Pa over the diastolic portion of the heart beat cycle. dPR is a resting index for the diagnostic of the severity of stenosis equivalent to iFR (instantaneous wave-Free Ratio).

iFR calculates the ratio of Pd and Pa over 75% of the diastolic portion. The accuracy, specificity and sensitivity of dPR compared to iFR as a reference standard1, using the same cut-off value of 0.89 and calculated from both CONTRAST2 and VERIFY 23 studies, are 97.1% [95.7%, 98.1% @95%CI], 95.9% [93.6%, 97.5% @95%CI] and 98.4 [96.6%, 99.3% @95%CI] respectively.

The diagnostic performance of dPR (cut-off=0.89) vs FFR (cut-off=0.80) compared to iFR (cut-off=0.89) vs FFR (cut-off=0.80) was also assessed. It was demonstrated that the diagnostic performance of dPR vs FFR is not statistically different from the diagnostic performance of iFR vs FFR, with 95% confidence interval significantly overlapping."

Opsens Submission for FDA Approval, see Complaint Exhibit C at p. 6.